REMARKS

Claims 1, 2 and 4-7 are pending in the application.

Reconsideration of the application is respectfully requested in view of the above amendments and the following remarks. For the Examiner's convenience, Applicant's remarks are presented in the order in which they were raised in the Office Action.

Claim Rejections Under 35 U.S.C. § 103

Claims 1, 2 and 4-7 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,728,534 (Mendelsohn et al.) in view of Sells et al.

Applicants respectfully traverse for reasons discussed below:

Independent claim 1 specifies a screening method for compounds that inhibit proliferation of vascular cells involving the steps of:

> (a) assessing an ability of a putative compound to inhibit induction of Egr-1, decrease expression of Egr-1 or decrease the nuclear accumulation or activity of the Egr-1 gene product.
>
> (b) assessing the ability of the putative compound to inhibit proliferation of vascular cells, and
>
> (c) selecting the putative compound that has been found to inhibit induction of Egr-1, decrease expression of Egr-1 or decrease the nuclear accumulation or activity of the Egr-1 gene product and inhibit proliferation of vascular cells.

Applicants submit that Mendelsohn et al. by itself or in combination with Sells et al. **does not** teach, suggest or provide any motivation for such a screening method.

The Examiner acknowledges the lack of Mendelsohn's teaching at page 3, paragraph 2 of the Office Action:

> "Mendelsohn et al. **does not** explicitly describe a method of screening for compounds that inhibit proliferation of cells selected from

> vascular smooth cells or endothelial cells, wherein the method specifically comprises **determining the ability of a putative compound to inhibit the induction of egr-1**"

The Examiner recognizes that Mendelsohn et al does not suggest assessing the ability of a putative compound to inhibit induction of Egr-1, decrease expression of Egr-1 or decrease the nuclear accumulation or activity of the Egr-1 gene product. Therefore, it is clear that **step a)** of the method of the invention is **not** contemplated by Mendelsohn et al.

The Examiner further acknowledges, at section 6 of the Office Action that:

> "It is **not specifically indicated** ... that the overall effect of decreasing egr-1 expression in these cells is inhibition of vascular endothelial and vascular smooth muscle cell proliferation"

Therefore, there is nothing in Mendelsohn et al. that explicitly suggests the link between inhibiting vascular cell proliferation and inhibiting Egr-1 activity. Hence, **step b)** of the present method involving assessing the ability of a putative compound to inhibit proliferation of vascular cells cannot be understood from the teachings of Mendelsohn et al.

The Examiner points to col. 11, lines 46-54 of Mendelsohn et al. to assert that the expected effect of a vasoprotective agent is a decrease in expression of egr-1 in both vascular smooth muscle cells and vascular endothelial cells. (Office Action, sections 5, page 4). However, Mendelsohn's "vasoprotective agents" **enhance** vascular endothelial cell activation. (col. 1, lines 43-63; Office Action, section 5, page 4). Therefore the reporter system for screening for vasoprotective agents in Mendelsohn et al. are not directed at Egr-1 inhibition as well as *inhibition* of vascular cell proliferation, as Mendelsohn's vasoprotective agents also enhance vascular endothelial cell activation.

Further, the stated purpose of Mendelsohn's patented invention (see Abstract) is to screen for agents that "activate estrogen responsive genes in vascular cells" as such agents are "potentially useful for treatment and prevention of vascular disease" **teaches away** from screening for agents that **inhibit** "estrogen responsive genes [such as egr-1] in vascular cells"

It follows that selecting a putative compound on the basis of its ability to inhibit induction of Egr-1, decrease expression of Egr-1 or decrease the nuclear accumulation or activity of the Egr-1 gene product **in combination** with its ability to inhibit proliferation of vascular cells (i.e., **step c**) is not disclosed or suggested by the teaching of Mendelsohn et al.

The Examiner cites Mendelsohn et al. for teaching the use of a reporter construct comprising an estrogen receptor responsive gene, wherein preferred vasoprotective agents are identified by their ability to influence the expression of an estrogen responsive gene. (Office Action pages 2-3).

Then, on pages 3-4 of the Office Action, the Examiner concludes that in view of Mendelsohn et al. and "[a]bsent evidence to the contrary one of ordinary skill in the art ... would have been motivated to design a reporter construct comprising either the egr-1 gene as a reporter gene ... to be used in a method for identifying compounds that inhibit proliferation of cells by determining the ability of said compound to inhibit or decrease the expression of the egr-1 reporter construct."

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. See In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). When determining obviousness, "the [E]xaminer can satisfy the burden of showing obviousness of the combination 'only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in art would lead that individual to combine the relevant teachings of the references.'" In re Lee, 277 F.3d 1338, 1343, 61 USPQ2d 1430, 1434 (Fed. Cir. 2002), citing In re Fritch, 972F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992).

The Examiner provides no objective teaching or general knowledge in the art at the time of the invention to combine two assays (inhibit egr-1 activity and inhibit proliferation of vascular cells) to arrive at a method for screening compounds that possess both properties. Therefore, Applicants submit that a prima facie case for obviousness has not been made.

At page 4 of the report, the Examiner asserts that:

> "It would have been obvious to one of ordinary skill in the art to **modify** the teachings of Mendelsohn et al. **to design** the methods of the claimed invention . . ."

The Federal Circuit Court of Appeals has repeatedly cautioned against employing hindsight by using the appellant's disclosure as a blueprint to reconstruct the claimed invention from the isolated teachings of the prior art. See, e.g., Grain Processing Corp. v. American Maize-Prods. Co., 840 F.2d 902, 907, 5 USPQ2d 1788, 1792 (Fed. Cir. 1988). Applicants submit that such "obvious to try" arguments with the benefit of the hindsight are improper.

The Examiner ignores the fact that a screen based on the ability of a compound to inhibit induction of Egr-1, decrease expression of Egr-1 or decrease the nuclear accumulation or activity of the Egr-1 gene product in combination with its ability of the same compound to inhibit proliferation of vascular cells is not disclosed or suggested by Mendelsohn et al. Therefore, it is not reasonable to expect that a person skilled in the art would be led to simply **modify** the teachings of Mendelsohn et al. to **design** the method of the invention. ("what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful ... ." In re O'Farrell, 853 F.2d 894, 903, 7 U.S.P.Q.2d 1673, 1681 (Fed. Cir. 1988) (citations omitted)).

Acknowledging that Mendelsohn et al does not specifically indicate that the overall effect of decreasing egr-1 expression in cells is inhibition of vascular endothelial and vascular smooth muscle cell proliferation, the Examiner refers to Sells et al. which discloses reduction of egr-1 expression in melanoma cells. The Examiner states that Sells et al. teaches that "inhibitors of EGR-1 function to inhibit the proliferation of tumor cells." (Office Action section 7, page 5). The Examiner asserts that it would have been obvious to modify the screen for vasoprotective agents taught by Mendelsohn with the teaching of Sells regarding the ability of egr-1 to inhibit proliferation of tumor cells to arrive at the claimed invention. Applicants respectfully traverse.

First, Sells et al. does not suggest or provide any one of the specific steps a) to c) of the method claimed. Sells et al. does not relate to the field of vascular diseases or methods of identifying agents that would be useful for treating vascular diseases. In fact, the document relates to the field of tumor biology, in particular the document concerns elucidating the role of Egr-1 in melanoma cells.

Second, Sells et al. does not relate to any methods of selecting compounds. Sells does not even provide methods of selecting compounds useful for inhibiting tumor cells. Further, the document does not suggest utilizing Egr-1 to select for compounds that can inhibit cell proliferation. Sells et al. is not relevant to the particular field.

Third, Mendelsohn et al. teaches vasoprotective agents that **activate estrogen responsive genes** in vascular cells. Mendelsohn also teaches vasoprotective agents that inhibit vascular smooth muscle cell activation and/or proliferation or **enhance vascular endothelial cell activation and/or proliferation**.

Thus Sells teaches away from combination with Mendelsohn. One of skill in the art would not have been motivated to combine the teaching of Sells to inhibit tumor cell growth with egr-1 inhibitors with the teaching of Mendelsohn to screen for vasoprotective agents that activate estrogen responsive genes in vascular cells.

A person of ordinary skill in the art must not only have had some motivation to combine the prior art teachings, but some motivation to combine the prior art teachings in the particular manner claimed. See, e.g., In re Kotzab, 217 F.3d 1365, 1371 (Fed. Cir. 2000) ("Particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed.")

A person skilled in the art would have known that vascular cells can not be expected to behave the same as tumor cells. In particular, tumor cells are understood to be abnormal cells characterized by uncontrollable growth properties. Accordingly, there is no certainty that results from the proliferation of tumor cells would be expected to apply to other types of normal cells.

Therefore, Applicants respectfully submit that the skilled artisan, with no knowledge of the claimed invention, would not have had an objective teaching or suggestion to combine the teachings of Sells et al. and Mendelsohn et al.

Further, even if the disclosures of Sells et al. and Mendelsohn et al. are combined, all limitations of the steps of the claimed method are not disclosed in these references. In particular, there is nothing in Mendelsohn et al. that emphasizes that of all the different classes of vasoprotective agents examined in this document, Egr-1 should be chosen to design a method of screening compounds that are capable of inhibiting vascular cell growth. Mendelsohn et al. does not show Egr-1 inhibition of cell proliferation in vascular cells. Moreover, although Sells et al. indicates that Egr-1 inhibits tumor cell growth, a skilled artisan would not simple extrapolate this to vascular cells without additional and undue experimentation.

Finally, Sells et al. and Mendelsohn et al by themselves or in combination do not disclose a method of screening for compounds involving testing of dual properties of a compound – its ability to inhibit proliferation of cells and its ability to inhibit Egr-1 activity.

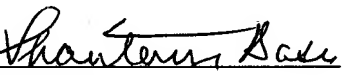
Therefore Applicants respectfully request that the rejection under § 103 over Mendelsohn et al. and Sells et al. be withdrawn.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to allow this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 529282000220. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: February 24, 2006

Respectfully submitted,

By 

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